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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/501,838	11/29/2004	Shmuel A. Ben-Sasson	24348-501 NATL	6386

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EXAMINER	
GUDIBANDE, SATYANARAYAN R	
ART UNIT	PAPER NUMBER
1654	

DATE MAILED: 02/07/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/501,838	BEN-SASSON ET AL.	
	Examiner	Art Unit	
	Satyanarayana R. Gudibande	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1,10-13,15-20,26,27,31-50,53-56,63 and 68-80 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1,10-13,15-18,26,27,31-38,53,68-75,77 and 78 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of group 16 directed to peptide sequence SEQ ID No. 16 in the reply filed on November 18, 2005 is acknowledged. The traversal is on the ground(s) that the applicants have amended the claims directed to a product, i.e., a penetrating module comprising specific peptides coupled to an effector, and hence unity of invention is established. This is not found persuasive because the disclosed products are peptides, and peptides have distinct structural features determined by their constituent amino acid sequences and have different properties, and none would render any of the other obvious. Hence the disclosed inventions lack unity of invention. Search for distinct compounds are conducted based on their structure-function relationship with regard to non-patented literature. Therefore, search for one compound would not lead to the discovery of another.

The requirement is still deemed proper and is therefore made FINAL.

Claims 19, 20, 39-50, 54-56, 76, 79 and 80 are withdrawn from consideration as being drawn to non-elected invention.

Allowable Subject Matter

Examiner searched Seq. ID Nos. 1-15 and 24-29 and found that Seq. ID Nos. 25-29 are free of art and therefore constitute allowable subject matter.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 34 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 34 contains the trademark/trade names for the non-ionic detergent poloxamer. Where a trademark or trade name is used in a claim as a limitation to identify or describe a particular material or product, the claim does not comply with the requirements of 35 U.S.C. 112, second paragraph. See *Ex parte Simpson*, 218 USPQ 1020 (Bd. App. 1982). The claim scope is uncertain since the trademark or trade name cannot be used properly to identify any particular material or product. A trademark or trade name is used to identify a source of goods, and not the goods themselves. Thus, a trademark or trade name does not identify or describe the goods associated with the trademark or trade name. In the present case, the trademark/trade name is used to identify/describe the species of several ethoxylated fatty acids and, accordingly, the identification/description is indefinite.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 10-13, 15-18, 26, 27, 31-38, 53, 68-75, 77 and 78 are rejected under 35 U.S.C. 103(a) as being unpatentable over EP 1 136 557 A1 of Schilfgaarde, et al., in view of Juliano, et al., Current Opinion in Molecular Therapeutics, 2000, 2, 297-303, in view of Lindgren, et al., TiPS, 2000, 21, 99-103, further in view of US 5,286,637 issues to Veronese.

In the instant application, applicants claim a penetrating module comprising a penetrating peptide and an effector that is coupled to the penetrating peptide, the penetrating peptide comprising an amino acid sequence represented by any one of SEQ ID No. 1-15 and 24-29, or any 12 contiguous amino acids of one of these sequences.

The amino acid sequence comprising the peptide sequence represented by SEQ ID No. 1 is known in the art (EP 1 136 557 A1 of Schilfgaarde, et al.,). Schilfgaarde, et al., teaches that the peptide sequence represented by SEQ ID No. 1 is involved in paracytosis through epithelial cell layers. The reference suggests methods for making paracytin fusion peptides via recombinant techniques with other biologically active peptides or proteins (page 9, lines 13-17) that could be used in therapeutic applications. However, the reference does not explicitly teach the fusion

peptide product that could be used in transport of therapeutically active agents across membrane barrier using a penetrating peptide.

Juliano, et al., teaches the use delivery peptides or penetrating peptides in transporting biologically active molecules across biological membranes. Reference teaches that chemically coupled peptide-oligonucleotide conjugates could be delivered into cytoplasm of cells using the penetrating peptides that are capable of crossing the membrane barrier (page 299, column 1).

Lindgren, et al., teaches that proteins, peptides, receptors, oligonucleotides, anti-sense DNA and PNA molecules can be coupled to cell penetrating peptides for transport across membrane (table 1 on page 100). They also suggest that cell-penetrating peptides can be designed and synthesized for cellular delivery of drugs and other research tools (Column 2, page 102).

Veronese teaches that, "Modification of biologically active substances such as peptide or proteins with [mPEG] is reported to change extensively their physical, chemical, enzymological, immunological, as well as their pharmacological and pharmacokinetic properties." (column 1, lines 15-19). Veronese teaches that, "Such modified peptide or protein derivatives exhibit some advantages when compared to the peptide or protein itself: increased water solubility, decreased antigenicity or increased half-life of the circulating peptide or protein." (column 1, lines 24-28).

The present invention claims a penetrating module comprising a penetrating peptide and an effector that is coupled or fused to at least one amino acid sequence selected from Seq. ID. Nos. 1-15 and 24-29, or any 12 contiguous amino acid residues of one of these peptides. Schilfgaarde, et al., suggests the methods for making paracytin fusion peptides via recombinant techniques with other biologically active peptides or proteins that could be used in therapeutic

applications. Juliano, et al., teaches the use of penetrating peptides for delivering biological effector molecules via chemical conjugation of the effector molecules to penetrating peptides. Lindgren, et al., have shown that biological molecules such as receptors, proteins, peptides, nucleic acid molecules and PNA can be linked to cell penetrating peptides. Therefore, it would be obvious form conjugates of biomolecules such as insulin that have therapeutic significance with penetrating peptides for the purpose of transporting across the biological membrane barrier as suggested by Juliano, et al. Veronese, et al., teaches pegylation of biomolecules and effect of pegylation on biophysical and biochemical properties biomolecules. Therefore, it would have been obvious to one of ordinary skill in the art to combine the teachings of Schilfgaarde, et al., Lindgren, et al., Juliano, et al., and Veronese, et al., to design a module of penetrating peptides conjugated to an effector molecule for transporting biologically active molecules across membranes.

One would have been motivated to make the conjugates of penetrating peptide with the effector molecule for the purpose of transporting biologically active compounds across the membrane barrier otherwise impervious to the molecule of interest.

One of ordinary skill in the art would have had a reasonable expectation for success in making the conjugate of an effector molecule with the penetrating peptides for the purpose of transporting biologically active substances into the cytoplasm of the cells. Therefore, it would have been prima facie obvious to one skilled in the art at the time the invention was made to design and develop a cell penetrating module for the delivery of therapeutic agents using a trans-membrane domain peptide in light of teachings of aforementioned references.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Satyanarayana R. Gudibande whose telephone number is 571-272-8146. The examiner can normally be reached on M-F 8-4.30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campell can be reached on 571-272-0974. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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